International Journal of Gynecology and Obstetrics 131 (2015) 54–58

Contents lists available at ScienceDirect

International Journal of Gynecology and Obstetrics

journal homepage: www.elsevier.com/locate/ijgo

www.figo.org

CLINICAL ARTICLE

Cumulative oxytocin dose during induction of labor according to maternal body mass index

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A R T I C L E I N F O

Article history:
Received 22 November 2014
Received in revised form 2 April 2015
Accepted 10 June 2015

Keywords:
Augmentation
Cesarean delivery
Induction of labor
Obesity
Oxytocin

A B S T R A C T

Objective: To determine the cumulative oxytocin dose needed to achieve vaginal delivery among obese and non-obese women. *Methods:* A retrospective study was undertaken of women with singleton, term (≥37 weeks) pregnancies who delivered at an institution in California, USA, between May 1 and July 31, 2012. Women were deemed to be obese when their body mass index (BMI; calculated as weight in kilograms divided by the square of height in meters) was 30 or above. Cumulative oxytocin doses were calculated for women who achieved vaginal delivery. *Results:* Overall, 413 women were included. Among 357 women for whom BMI data were available, 204 (57.1%) were obese. Vaginal delivery was achieved in 379 women. Among women who received augmentation after spontaneous labor onset, obese women trended towards more cumulative oxytocin (minimum: 24.7 ± 100.5 mU among women with a BMI of 18.50–24.99; maximum: 1580.5 ± 2530.5 mU among women with a BMI of 35.00–39.99; $P = 0.086$). Women who underwent induction of labor required significantly more oxytocin with increasing BMI class ($P < 0.001$), despite no difference in length of labor. *Conclusion:* Obese women required a larger cumulative oxytocin dose to achieve vaginal birth during labor induction, but not during augmentation of labor. The physiology of spontaneous labor could supersede or influence the metabolic derangement facing obese patients undergoing induction of labor.

1. Introduction

Obesity is a risk factor for cesarean delivery: with increasing weight, the odds of a cesarean delivery can more than double [1–3]. Contemporary analyses suggest that a protracted first stage of labor is more common among obese women than among women of a normal weight, and that the second stage of labor progresses more slowly [4–8]. The average progress during labor in obese women can be interpreted as a labor arrest disorder, which is one of the major contributing indications for preventable primary cesarean in the USA [9–11].

The reasons behind the slower progress in labor among obese women remain unknown. Increasing evidence suggests that a complex interplay of hormonal modulators produced in adipose tissue could inhibit myometrial contractility [12–14]. In vitro studies also suggest that oxytocin receptor expression and/or function is affected by body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters) and that oxytocin response is somehow blunted by obesity [15]. Indeed, treatment of protracted labor with oxytocin has been shown to be less effective in obese patients [16].

The objective of the present study was to assess the cumulative oxytocin dose needed to achieve vaginal delivery among obese and non-obese women after spontaneous onset of labor or labor induction. The low primary cesarean delivery rate in the study center makes for an ideal setting to study the cumulative oxytocin dose required for vaginal birth.

2. Materials and methods

A retrospective study was undertaken of women who delivered at Arrowhead Regional Medical Center (ARMC), Colton, CA, USA, between May 1 and July 31, 2012. The ARMC performs approximately 2500 deliveries annually and serves as a tertiary referral center for complicated pregnancies within the County of San Bernardino, CA. Viable singleton pregnancies at term (37–42 weeks) with cephalic presentation were included. Women with a previous cesarean delivery, multiple pregnancy, or abnormal placentation, and those undergoing primary cesarean delivery for maternal or fetal indications that would contraindicate vaginal delivery (i.e. breech) were excluded. The study was conducted with the approval of the ARMC Institutional Review Board. Informed consent was not required or obtained because of the retrospective nature of the study.

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http://dx.doi.org/10.1016/j.ijgo.2015.04.038

Charts were reviewed and the following data were retrieved: BMI at time of delivery, method of delivery, use of oxytocin (as augmentation [among women with spontaneous onset of labor] compared with induction), age, gravidity, parity, gestational age, birth weight, Apgar score, umbilical cord arterial pH, cervical examination at time of admission, maternal medical comorbidities, indication for induction, and cumulative oxytocin dose. BMI was calculated based on delivery weight and height, as pre-pregnancy weight is performed by recall and subject to a greater degree of bias. Pregnancies were classified as high risk when the mother had one or more significant comorbid condition that could increase the odds of cesarean delivery, including diabetes (gestational or pre-existing), intrauterine growth restriction, hypertension, pre-eclampsia, anemia (hemoglobin <100 g/L), asthma, use of illicit substances, infections with herpes simplex virus, heart disease, hospitalization during pregnancy, lupus, seizure disorder, advanced maternal age (age 35 years or greater at time of delivery), or other maternal or fetal condition. The WHO International Classification of Obesity was used to define five BMI classes: normal weight (18.50–24.99), pre-obese (25.00–29.99), obesity class I (30.00–34.99), obesity class II (35.00–39.99), and obesity class III (≥40.00). Spontaneous labor was defined by regular uterine contractions with cervical dilation of 3 cm or more on digital examination, irrespective of effacement, or documented cervical change in the presence of uterine contractions if cervical dilation was less than 3 cm.

Oxytocin augmentation was started under the direction of the on-call attending physician if inadequate contractions were present (<4 contractions in a 10-minute period or <200 Montevideo units [MVU]) with a lack of cervical dilation or fetal descent, after the onset of spontaneous labor. The ARMC standard practice in patients with an arrest of labor follows evaluation of estimated fetal weight and clinical pelvimetry, placement of internal monitors if not contraindicated, and oxytocin infusion to treat inadequate contractions, aiming for 200–250 MVU. Thus, for labor augmentation, oxytocin was started at a rate of 1–2 mU per minute and increased by 1–2 mU per minute every 20–30 minutes. For labor induction, cervical ripening was performed at the discretion of the attending physician using 25–50 μg misoprostol by oral or vaginal route every 4–6 hours, transcervical Foley bulb ripening, oxytocin according to the labor augmentation titration schedule, or through a sequential combination of methods. Oxytocin was started following cervical ripening at the discretion of the attending physician. A minimum of 4 hours since misoprostol administration was required before oxytocin initiation. If transcervical ripening was used, oxytocin administration was started after expulsion of the catheter.

Comparisons were made between four subgroups within the cohort, defined as: BMI below 30, spontaneous labor; BMI of 30 or above, spontaneous labor; BMI below 30, induction of labor; and BMI of 30 or above, induction of labor. Perinatal characteristics between the four groups were compared using the Student *t* test and χ^2 test as appropriate. The Levene test for equality of variances was used to determine use of the *t* test for equal or unequal variances. The Fisher exact test was used to compare the frequency of high-risk pregnancies, and use of oxytocin among induced patients.

Cumulative oxytocin doses were compared in augmented patients and in those who underwent induction of labor on the basis of BMI class using univariate ANOVA testing. One outlier, with a BMI of 36.2, was excluded from the analysis because the cumulative oxytocin dose was extremely high (675,000 mU). Least-square difference testing was used to compare the five BMI classes. Only women who achieved vaginal delivery were included in the analysis of cumulative oxytocin dose, because cesarean delivery for either failure to progress or category 2/3 fetal heart rate tracing interrupted the exposure and falsely decreased the cumulative doses.

Initial cervical examinations were also compared for the four groups using a modification of the Bishop score. Position and consistency were not reliably recorded in the medical record; therefore, dilation, effacement, and station were used to create a score ranging from 0 to a maximum of 9.

The duration of labor was determined to assess whether any increased oxytocin dose was due to a longer labor, and therefore a longer duration of exposure to oxytocin alone, rather than an increased need for oxytocin. The first and second stages of labor were considered to be from 6–10 cm dilation and from 10 cm to delivery, respectively. The total time for active labor was defined as the sum of the first and second stages, or the time from 6 cm to delivery. The duration of labor was compared for the first, second, and active stages for each BMI class, on the basis of the onset of labor (spontaneous or induction), using a univariate ANOVA test.

All analyses were performed using SPSS version 22.0.0.0 (IBM, Armonk, NY, USA). $P < 0.05$ was considered statistically significant.

3. Results

In total, 413 women were included. Among these women, 265 (64.2%) were admitted with spontaneous labor and 148 (35.8%) underwent labor induction. A primary cesarean delivery was performed in 34 (8.2%) women. Oxytocin was administered to 262 (63.4%) women. Primary cesarean delivery was more frequent among women who received oxytocin (31 [11.8%] of 262) than among those who did not receive oxytocin (3 [2.0%] of 151; $P = 0.002$).

Overall, 204 (57.1%) of 357 women for whom BMI was available were obese (Table 1). Cesarean delivery was more common among obese women (21 [10.3%] of 204) than among women with a BMI below 30 (10 [6.5%] of 153), although the difference was not significant

Table 1
Demographic and perinatal characteristics of all included women.[a]

Characteristics	Value (n = 413)
Age, y	25.24 ± 6.19
Gravidity	2.74 ± 1.85
Parity	1.25 ± 1.48
Ethnic origin[b]	
White	30 (9.6)
Hispanic	236 (75.6)
Black	29 (9.3)
Asian	6 (1.9)
Other	11 (3.5)
Length of pregnancy, wk	39.4 ± 1.2
BMI	32.12 ± 6.76
High-risk pregnancy	266 (64.4)
WHO obesity class[c]	
Normal	39 (10.9)
Pre-obese	114 (31.9)
Obese, class I	100 (28.0)
Obese, class II	65 (18.2)
Obese, class III	39 (10.9)
Admission cervix examination	
Cervix dilation	2.79 ± 1.91
Cervix effacement	67.05 ± 25.86
Fetal station	–1.5 ± 0.9
Bishop score (modified)	5.27 ± 1.84
Oxytocin	
No	151 (36.6)
Yes	262 (63.4)
Type of delivery	
Spontaneous vaginal	360 (87.2)
Operative vaginal	19 (4.6)
Cesarean	34 (8.2)
Neonatal characteristics	
Birth weight, g	3332 ± 419
5-minute Apgar score	8.92 ± 0.36
Umbilical artery pH	7.26 ± 0.07

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters).
[a] Values are given as mean ± SD or number (percentage).
[b] n = 312.
[c] n = 357.

($P = 0.403$). Delivery was by cesarean for 2 (5.1%) of 39 women of normal weight, 8 (7.0%) of 114 in the pre-obese group, 9 (9.0%) of 100 in obesity class I, 5 (7.7%) of 65 in obesity class II, and 7 (17.9%) of 39 in obesity class III. In all women, use of oxytocin was more common among obese women (146 [71.6%] of 204) than among non-obese women (80 [52.3%] of 153; $P = 0.003$).

Among women with a spontaneous onset of labor, obese women were more likely to receive oxytocin augmentation ($P = 0.02$), be older ($P = 0.037$), and have neonates with higher birth weights ($P = 0.004$) than were non-obese women, but surprisingly, fewer were noted to be high risk ($P = 0.013$) (Table 2). The remaining spontaneous labor characteristics analyzed were similar between obese and non-obese women (Table 2).

With regard to women who underwent labor induction, there were no notable differences in the demographic and perinatal characteristics between obese and non-obese women, except for the findings that more obese women had received oxytocin ($P = 0.036$) and that obese women delivered neonates with a higher birth weight ($P = 0.008$) (Table 2). Few obese women achieved labor using ripening methods alone (Table 3). There was no difference between women with a BMI below 30 and women with a BMI of 30 or above with regard to the use of cervical ripening methods (Table 3). Indications for induction did not differ between obese and non-obese women ($P = 0.99$) (Table 4).

Among the 34 women who underwent cesarean delivery, the indication was category 2/3 fetal heart rate for 20 (58.8%), failure to progress for 13 (38.2%), and hemorrhage for 1 (2.9%). Further, the indication for cesarean delivery did not depend on obesity ($P = 0.755$).

The mean cumulative oxytocin dose for the 379 women who delivered vaginally was 2270 ± 4226 mU (range 13–29 972). Among women who received augmentation, there was a non-statistically

Table 3
Methods of cervical ripening among women who underwent induction.[a]

Method of cervical ripening	BMI <30 (n = 40)	BMI ≥30 (n = 61)	*P* value
Misoprostol	22 (55.0)	36 (59.0)	0.798
Misoprostol and Foley catheter	0	1 (1.6)	
Foley catheter	2 (5.0)	2 (3.3)	
Oxytocin	14 (35.0)	17 (27.9)	
Amniotomy	2 (5.5)	5 (8.2)	

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters).
[a] Values are given as number (percentage) unless indicated otherwise.

Table 2
Characteristics among the four subgroups.[a]

Characteristic	Spontaneous onset of labor[b]			Induction of labor[c]		
	BMI <30 (n = 102)	BMI ≥30 (n = 122)	P value	BMI <30 (n = 51)	BMI ≥30 (n = 82)	P value
Cesarean delivery	4 (3.9)	8 (6.6)	0.336	6 (11.8)	14 (17.1)	0.475
Age, y	24.04 ± 5.69	25.70 ± 6.05	0.037	24.29 ± 7.00	26.38 ± 6.96	0.096
Gravidity	2.66 ± 1.71	3.01 ± 1.94	0.115	2.33 ± 1.84	2.67 ± 1.92	0.318
Parity	1.28 ± 1.35	1.35 ± 1.43	0.716	0.88 ± 1.31	1.13 ± 135	0.292
Ethnic origin[d]			0.300			0.892
White	5/12 (41.7)	7/12 (58.3)		7/16 (43.8)	9/16 (56.3)	
Hispanic	53/127 (41.7)	74/127 (58.3)		26/70 (37.1)	44/70 (62.9)	
Black	11/19 (57.9)	8/19 (42.1)		2/8 (25.0)	6/8 (75.0)	
Asian	5/6 (83.3)	1/6 (16.7)		0	0	
Other	1/4 (25.0)	3/4 (75.0)		2/4 (50.0)	2/4 (50.0)	
Gestational age, wk	39.1 ± 1.1	39.4 ± 1.1	0.095	39.6 ± 1.4	39.7 ± 1.4	0.923
High-risk pregnancy	82 (80.4)	83 (68.0)	0.013	26 (51.0)	34 (41.5)	0.159[f]
BMI	26.12 ± 2.45	36.88 ± 4.88	<0.0011	26.93 ± 2.42	37.21 ± 6.70	<0.001
WHO obesity class						
Normal	28 (27.5)	0		11 (21.6)	0	
Pre-obese	74 (72.5)	0		40 (78.4)	0	
Obesity class I	0	61 (50.0)		0	39 (47.6)	
Obesity class II	0	42 (34.4)		0	23 (28.0)	
Obesity class III	0	19 (15.6)		0	20 (24.4)	
Cervix characteristics on admission						
Dilation, cm	3.8 ± 1.9	3.4 ± 1.8	0.105	1.4 ± 1.0	1.2 ± 0.9	0.096
Effacement, %	73.7 ± 24.7	74.2 ± 23.3	0.876	56.3 ± 22.4	51.1 ± 24.5	0.224
Fetal station[e]	–1.2 ± 0.9	–1.4 ± 0.9	0.115	–1.9 ± 0.9	–2.1 ± 0.9	0.171
Bishop score (modified)	6.1 ± 1.5	5.9 ± 1.5	0.308	3.9 ± 1.4	3.5 ± 1.3	0.114
Oxytocin use						
No oxytocin	67 (65.7)	56 45.9)	0.002	6 (11.8)	2 (2.4)	0.036[f]
Oxytocin	35 (34.3)	66 (54.1)		45 (88.2)	80 (97.6)	
Type of delivery						
Spontaneous vaginal	91 (89.2)	110 (90.2)	0.336	44 (86.3)	65 (79.3)	0.530
Operative vaginal	7 (6.9)	4 (3.3)		1 (2.0)	4 (4.9)	
Cesarean	4 (3.9)	8 (6.6)		6 (11.8)	14 (17.1)	
Neonatal characteristics						
Birth weight, g	3252 ± 376	3415 ± 419	0.004	3141 ± 483	3371 ± 439	0.008
5-minute Apgar score	8.9 ± 0.5	8.9 ± 0.3	0.706	8.9 ± 0.1)	8.9 ± 0.4)	0.058
Umbilical artery pH	7.28 ± 0.07	7.26 ± 0.07	0.050	7.26 ± 0.06	7.25 ± 0.07	0.181
Length of labor, min						
First stage	170.8 ± 140.5	161.3 ± 129.4	0.651	181.2 ± 187.7	153.7 ± 144.7	0.440
Second stage	37.2 ± 45.6	38.5 ± 51.7	0.870	52.5 ± 50.6)	47.8 ± 47.5	0.637
Active labor	207.5 ± 160.7	200.2 ± 152.3	0.764	233.7 ± 201.1	201.1 ± 163.9	0.383

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters).
[a] Values are given as number (percentage), mean ± SD, or number/total number (percentage), unless indicated otherwise.
[b] Data for BMI missing for 41 women.
[c] Data for BMI missing for 15 women.
[d] Data for ethnic origin missing for 69 women.
[e] –5 to +5
[f] Fisher exact test.

Table 4
Indications for induction of labor.[a]

Indication	Total (n = 134)	BMI <30 (n = 53)	BMI ≥30 (n = 81)
Pre-eclampsia	33 (24.6)	9 (17.0)	24 (29.6)
Post-dates	28 (20.9)	13 (24.5)	15 (18.5)
Oligohydramnios	20 (14.9)	11 (20.8)	9 (11.1)
Maternal medical complication	15 (11.2)	5 (9.4)	10 (12.3)
Rupture of membranes	11 (8.2)	3 (5.7)	8 (9.9)
Diabetes	8 (6.0)	1 (1.9)	7 (8.6)
Non-reassuring fetal status	8 (6.0)	3 (5.7)	5 (6.2)
Intrauterine growth restriction	6 (4.5)	5 (9.4)	1 (1.2)
Vaginal bleeding	2 (1.5)	0	2 (2.5)
Elective[b]	3 (2.2)	3 (5.7)	0

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters).
[a] Values are given as number (percentage).
[b] Elective induction performed at patient request; ≥39 weeks of pregnancy without medical or obstetric indication.

significant trend toward higher oxytocin doses with increased BMI class (minimum: 24.7 ± 100.5 mU among women with a normal weight; maximum: 1580.5 ± 2530.5 mU among women in obesity class II; $P = 0.086$) (Fig. 1). However, even though there were no significant differences in the duration of the first or second stages of labor, and despite having a slightly shorter overall length of labor, women who underwent induction required a significantly increased oxytocin dose with increasing BMI class ($P < 0.001$; adjusted $R^2 = 0.194$). Among induced women, least-squares difference analysis showed that the cumulative dose between normal-weight and pre-obese women was not significantly different ($P = 0.373$). However, women of a normal weight required significantly less oxytocin than did women in obesity class I or III ($P = 0.010$ and $P = 0.020$, respectively), with a trend toward less oxytocin use when compared with women in obesity class II ($P = 0.054$). Women in the pre-obese group required significantly less oxytocin than did women in obesity class III ($P = 0.047$). However, no significant differences were recorded between women in obesity class III and those in class I ($P = 0.792$) or class II ($P = 0.474$). For each step increase in WHO obesity class, women required between 445 mU (class I to class II; $P = 0.54$) and 1494 mU (pre-obese to class I; $P = 0.016$) more oxytocin. Women in obesity class III required 2489 mU more oxytocin than did women of a normal weight.

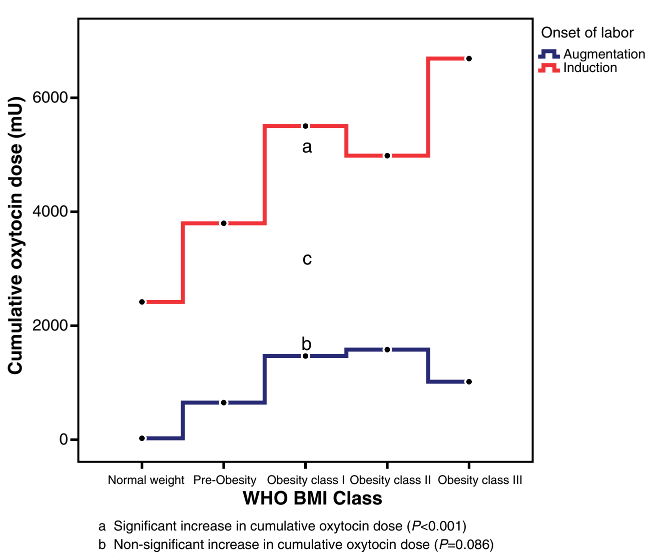

Fig. 1. Cumulative oxytocin dose according to WHO obesity class in women who had spontaneous labor or induction of labor. Abbreviation: BMI, body mass index.

4. Discussion

The present results indicate that obese women who undergo induction of labor require incrementally more cumulative oxytocin as their BMI class increases; nevertheless, obese women whose spontaneous labor is augmented do not require more cumulative oxytocin to achieve vaginal delivery. The indication for induction and starting Bishop scores were similar for obese and non-obese women, suggesting the higher cumulative oxytocin dose is a result of increased weight. Previous research on oxytocin use in obese patients has focused on oxytocin requirements during labor (mU/minute) as opposed to the cumulative doses needed to achieve vaginal delivery [17,18]. However, the high probability of cesarean delivery—reported to be up to 70% in women in obesity class III in one review [16]—has impeded the quantification of cumulative oxytocin requirements. Because the ARMC has a low cesarean rate and given that an increased likelihood of cesarean delivery with increasing BMI class was not observed in the present study, the results make it possible to quantify and compare the oxytocin doses required to achieve vaginal delivery in induced and augmented women by BMI class.

The hormonal milieu of an obese woman appears to interact with oxytocin regulation and response, and/or affect myometrium contractility. It is possible that increased BMI leads to variation in expression and function of the oxytocin receptor of the human myometrium [15], which explains the higher doses of oxytocin required in obese patients. Further, leptin, methyl palmitate, and apelin are overexpressed in obese women, and have all been shown to impact myometrium contractility [12–14]. The present results showed that, among women with augmented labor, obesity was not associated with higher oxytocin doses. Perhaps the physiology of spontaneous labor supersedes or changes the metabolic derangement facing the obese patient undergoing induction of labor. This would also explain previous results indicating a lack of difference in myometrium contractility in response to oxytocin on the basis of BMI [19]; as the present results suggest, the myometrium contractility of augmented and induced women could be different. Thus, the impact of BMI on oxytocin receptor function or upregulation, in the context of known hormonal variants in obese women, in the setting of induction compared to augmented labor would be an interesting investigation.

The reason for fewer high-risk pregnancies in obese women with spontaneous labor compared with non-obese women with spontaneous labor is unknown, but could reflect a difference in the type of high-risk conditions experienced by women with a BMI below 30 and those who are obese. Perhaps the nature or severity of the high-risk condition in an obese woman predisposes her to spontaneous labor before an indicated scheduled induction date.

A major strength of the present study is the large proportion of women who were obese at a center with a low primary cesarean delivery rate, which allowed an appropriate assessment of the cumulative oxytocin dose according to WHO BMI class in women with an adequate opportunity to deliver vaginally. The main limitation of the present review is the lack of an evaluation of other medications used during labor, such as magnesium sulfate, which can affect labor progression. Further, given the retrospective nature of this review, it was not possible to control for methods of induction; although the cervix ripening methods used were similar between obese and non-obese women, the effect of method of induction on oxytocin use could not be determined. Additionally, possible complications, such as postpartum hemorrhage in women with a higher cumulative oxytocin dose (a known risk), were not assessed. Finally, a standard low-dose oxytocin protocol was used; therefore, it is unclear if labor could be achieved more expediently in obese women using higher dose titrations.

The intention of the present study was not to determine the reasons behind the achievement of a low primary cesarean delivery rate, but instead to take advantage of this fact to quantify the cumulative doses of oxytocin required to achieve vaginal delivery. For all pregnancies delivered in the study period at any gestational age, the primary cesarean delivery rate was 13% (preterm birth was excluded in the analysis above);

the US national primary cesarean delivery rate ranges from 13% to 20.6% [20,21]. Obesity was not a risk factor for cesarean delivery at ARMC during the study period. Despite delivering neonates with a higher mean birth weight, 90% of obese women were able to achieve vaginal delivery in the same average time as the non-obese cohort.

A very low primary cesarean delivery can be obtained in part by attaining adequate labor during induction, which could entail increased cumulative doses of oxytocin as BMI increases. Obese women required a larger cumulative oxytocin doses to achieve vaginal birth during labor induction. Nevertheless, higher oxytocin doses were not required for obese women when their labor was augmented.

Conflict of interest

The authors have no conflicts of interest.

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